Glandular odontogenic cyst associated with ameloblastoma: Case report and review of the literature

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Abstract
Glandular odontogenic cyst (GOC) associated with ameloblastoma is an exceedingly rare histologic presentation with no known clinical significance or treatment applications. Four cases have been reported, three in the mandible and one in the maxilla. The age range is 14-65 and with male predilection. All four presented with swellings and two with pain. We add one more case to the literature of a 58-year old male presenting with an expansile multilocular radiolucency between teeth #19-23. The ameloblastomatous changes in this case are consistent with those of a unicystic ameloblastoma-mural subtype. Although the histologic changes are those of a unicystic ameloblastoma, the clinical and radiographic findings are not. This case therefore presents a clinical challenge with regards to treatment planning for recurrence and prognosis. We conclude that treatment for GOC therefore be based on individual clinical presentation.

Key words: Glandular odontogenic cyst, GOC, ameloblastoma, unicystic ameloblastoma, mural unicystic ameloblastoma.

Introduction
Glandular odontogenic cyst (GOC) is an uncommon odontogenic cyst with an incidence of 0.12-0.2% of odontogenic cysts (1-3). The histological criteria for GOC have evolved since it was first described by Gardner et al. in 1988 and its diagnosis is less of a challenge today in light of an increasing number of reports and clearer definition of its diagnostic criteria (2,4,5). GOC has been traditionally described as predominantly affecting middle-aged individuals in their 4th-7th decades of life (mean=45.9 years-old) (2,3). While some studies report no significant gender predilection (1,3,6–8), others have reported a slight male predominance of 1:3.1 to 2:1 (2,9,10). GOC commonly affects the mandible 2-3x as often as it does the maxilla (1,2,7,8,10). Some reports claim a preference for the anterior mandible (3,6,8), but others indicate equal distribution between anterior and posterior mandibular segments (2). The radiographic...
findings of GOC often resemble those of odontogenic keratocyst or ameloblastoma, the former presenting as a unilocular radiolucency with scalloped borders and the latter as a multilocular and expansile radiolucency (1). Histologically, GOC may have features overlapping with botryoid odontogenic cyst, dentigerous cyst, and low-grade mucoepidermoid carcinoma (2,8), but not with ameloblastoma.

Ameloblastoma are described as the most frequently diagnosed odontogenic tumor (11) and often arise with clinical and radiographic features reminiscent of odontogenic cysts, including dentigerous cyst (12). Unicystic ameloblastoma (UA) is a frequent variant of ameloblastoma arising in a cystic structure. It is most commonly diagnosed in the second decade of life and has a strong predilection for the mandible (12). Unicystic ameloblastoma commonly presents as a unilocular radiolucency with corticated border with 50-80% associated with impacted third molars, closely resembling dentigerous cyst (12).

The connection between unicystic ameloblastoma and GOC has not been well established given the rarity of the condition. So far, only four cases of GOC are reported to be associated with ameloblastoma (4,13-15). None of the four reports have clearly defined the type of ameloblastoma present within the GOC lesion, but at least three point to unicystic ameloblastoma (4,13,14). In this manuscript, we present a case of GOC associated with clear ameloblastomatous changes consistent with those of the unicystic ameloblastoma-mural histologic subtype. We do not however have enough information to determine clinical behavior, treatment, or prognosis.

Case Report

- Clinical Findings
A 58-year-old male presented with a slowly expansile lesion in the left posterior mandible which had been present for an unknown period. The teeth were vital and pushed apart, especially in the area of #21 and 22 (Fig. 1). The swelling was clinically obvious, protruding lingually into the floor of mouth and expanding buccally into the mandibular vestibule (Fig. 2). The swelling reflected buccally as translucent grey-blue through the mucosa (Fig. 2). The patient denied pain or paresthesia.

Radiographic Findings
Radiographically, a large, multilocular radiolucency with scalloped borders was present between teeth #19-23. The margins are clearly defined. Teeth #21 and #22 are clearly pushed apart. Tooth resorption was not identified and there was no evidence of alveolar bone perforation (Fig. 1).

Histological Findings
The hematoxylin and eosin (H&E) stained sections of an incisional biopsy showed a combined cystic and solid neoplastic process. The cystic structure had features of GOC in that the epithelium was of variable thickness (Fig. 3A), had glandular-like spaces within the lining epithelium (Fig. 3B), scant mucous producing cells which were positive with mucicarmine stain (Fig. 3D), and cuboidal epithelial cells with hobnail appearance layering the very superficial layer of the lining epithelium (Fig. 3C). In rare areas, epithelial spheres were noted (Fig. 3C).

The second component was the neoplastic ameloblastomatous changes which manifested in two forms (Fig.
First, there were multifocal ameloblastomatous changes involving the deep layers of the lining epithelium including the basal cell layer (Fig. 3E). The latter was cuboidal, palisaded with focal reverse polarization. The basal cell layer was covered by stellate-reticulum type of epithelial cells. The connective tissue wall contained odontogenic epithelial neoplastic islands of variable shapes and sizes (Fig. 3F). The epithelial islands had follicular, acanthomatous and combined histologic morphology. The periphery of the islands was lined by one layer of palisaded cuboidal/columnar cells with reverse polarization typical of ameloblastoma histologic features.

**Discussion**

The association of ameloblastoma with GOC is exceedingly rare. Only four such cases exist in the literature making the current case only the fifth to be reported. A review of the literature is presented in Table 1, summarizing the clinical and radiographic presentation of all five cases (4,13-15).

Clinically, three of the four cases occurred in the pos-
terior mandible extending anteriorly (4,13,14), and one occurred in the posterior maxilla, again extending ante-
riorly (15). The current case was also in the mandible 
between teeth #19-23, resulting in a mandible to maxilla 
ratio of 4:1. Of those cases occurring in the mandible, all 
three affected the right side (4,13,14), but one origina-
ted from tooth #19 (left mandible) and extended to tooth 
#27 (4). The current case was on the left side of the jaw. 

In the maxilla, the reported case was located between 
the left central incisor to the right first molar (15). All 
four cases and the current case presented with extensive 
swelling and expansion, and three cases presented with 
pain (13-15). The teeth in the current case were all vital, 
a characteristic observed in only one of the four cases 
previously reported (14). The age range for the four re-
ported cases is 14-65 (mean=36-years-old) with a male 
to female ratio of 3:1 (4,13-15). The present case is that 
of a 58-year-old male, older than the mean age, but wi-
thin the age range described in the literature.

Radiographically, all four cases including the present 
one were radiolucent and expansile. Three of the pre-
viously reported cases were unilocular (4,13,14), and 
one was multilocular (15). The current case was also 
multilocular. Root resorption was described in two of 
the four cases (13,14); the current case did not show root 
resorption. Three cases demonstrated displacement of 
teeth and so did the current case (13-15). Finally, two 
cases were described to perforate either or both the buc-
cal or lingual plate (14,15). The current case did not per-
forate bone.

Histologically, the current case demonstrates clear chan-
ge from cyst to neoplasm within the lining epithelium 
(Fig. 3); such clear change is also noted in three of the 
reported cases (13-15). Gardner only described odonto-
egenic epithelial islands in the wall of cyst (4). The cu-
temporary case shows the presence of odontogenic epithelial 
changes arising only in the lining epithelium (13). 

Thus far, two of the reported cases as well as the current 
case show ameloblastomatous changes arising in the li-
ning epithelium with a solid epithelial island component 
in the connective tissue wall (14,15). These features are 
consistent with those of unicystic ameloblastoma-mural 
subtype and widely described to occur in dentigerous 
cysts (12).

None of the four reported cases commented on the cli-
nical behavior of such histologic changes within GOC, 
neither did these reports address prognosis and recur-
rence rate. It is too soon for treatment, prognosis, and recu-
rence to be predicted on such a small sample. As such, 
data from ameloblastoma arising in dentigerous cyst 
should not be extrapolated to GOC associated amelo-
blastoma. These two cysts differ widely in their clinical, 
radiographic, or histologic presentations, and even more

<table>
<thead>
<tr>
<th>Reference No.</th>
<th>Age/Gender</th>
<th>Site</th>
<th>Clinical</th>
<th>Radiographic</th>
<th>Histology</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>19/M</td>
<td>L Mand.</td>
<td>Swelling</td>
<td>Unilocular RL</td>
<td>Neoplastic odontogenic epithelial islands in the connective tissue wall.</td>
</tr>
<tr>
<td>13</td>
<td>14/M</td>
<td>R Mand.</td>
<td>Swelling/Pain/ Non-vital teeth</td>
<td>Unilocular RL/ Root Resorption/ Tooth displacement</td>
<td>Ameloblastomatous changes within the lining epithelium only.</td>
</tr>
<tr>
<td>14</td>
<td>45/F</td>
<td>R Mand.</td>
<td>Swelling/Pain/ Tooth mobility</td>
<td>Unilocular RL/ Bone perforation/ Root Resorption</td>
<td>Ameloblastomatous changes in the lining epithelium and neontogenic epithelial islands in the connective tissue wall.</td>
</tr>
<tr>
<td>15</td>
<td>65/M</td>
<td>R Max.</td>
<td>Swelling/Pain/ Tooth exfoliation</td>
<td>Multilocular RL/ Bone perforation</td>
<td>Ameloblastomatous changes in the lining epithelium and neoplastic odontogenic epithelial islands in the connective tissue wall.</td>
</tr>
</tbody>
</table>

R=Right; L=Left; RL=radio-
certainly in their behavior, prognosis, and recurrence rate.

In conclusion, we present a case of ameloblastoma associated with GOC in a 58-year-old male who presented with extensive expansion of the mandible with a multilocular radiolucent radiographic appearance.

References

Message of the manuscript
This study highlights the clinical and pathologic features of a rare glandular odontogenic cyst associated with ameloblastoma as seen in the Pacific Northwest.

Conflicts of interest and disclosure
No conflicts of interest to disclose.